

XXII. "The Physiological Action of Atropine, Digitaline, and Aconitine on the Heart and Blood-vessels of the Frog." By FREDERIC B. NUNNELEY, M.D. Lond. Communicated by Dr. BASTIAN. Received June 16, 1869.

(Abstract.)

These experiments were undertaken with the view of determining more exactly the physiological action of atropine, digitaline, and aconitine on the heart and blood-vessels, by methods of experiment which have hitherto been little followed out.

My experiments on atropine have led me to the conclusion that it exerts no action on the blood-vessels, a result which differs from that of Mr. Wharton Jones and of M. Meuriot. This opinion was adopted after a lengthened examination of the natural circulation in the frog's web, and of the numerous spontaneous changes which it undergoes, and also of those which are the result of the slightest irritation. It is some of these changes which have, I think, been assigned by the observers just named to the special action of atropine.

Different opinions have been entertained with regard to the action of digitaline on the heart; the result of my observations is given below. Aconitine has also a very marked action on the heart, the opposite of that of digitaline; its physiological effects are stated.

In actually conducting the experiments, the general symptoms of a poisonous dose were first observed, so as to show the period at which the heart lost its vitality in relation to the rest of the body.

Next, the visible effect produced on the heart, exposed *in situ*, was noted as regards the quality, frequency and rhythm of its contractions; and also the alteration seen to occur in a heart removed from the body and immersed in a solution of the alkaloid.

Lastly, the effect on the blood-vessels of the web, was examined with the aid of the microscope.

The results obtained have been thrown into the form of conclusions.

Atropine, digitaline, and aconitine do not produce any effect on the vessels of, or circulation in, the frog's web, whether locally applied in the form of solution, or injected under the skin at a distant part, so as to influence the animal generally; in the latter case, as they tend to impair or abolish the functions of the heart, the circulation necessarily undergoes secondary changes; but these alterations do not occur until the *heart* is visibly affected.

*Atropine.*—1. A few minutes after a dose of about  $\frac{1}{20}$  gr., the frog becomes quiet, sinks down on the plate containing it and makes ineffectual efforts to jump, the respiratory movements cease and it dies in from  $1\frac{1}{2}$  to 3 hours. On exposing the heart, it is found beating, and the contractions continue for some hours.

2. The action of atropine on the heart is neither considerable nor ener-

getic, a progressive weakening of its power being the most prominent visible effect. The heart continues to beat for some time after the manifestations of life in the rest of the animal have disappeared; finally it slowly dies itself, the ventricle being left in a state of relaxation; this occurs at the end of ten, twelve, or several more hours.

3. The heart's contraction gradually decreases in frequency and there is no primary acceleration.

The rhythm of the heart's action is not interfered with; the auricles continue to beat for some time after the ventricle has ceased to do so.

4. When the heart is removed from the body and immersed in a solution of sulphate of atropine, it ceases to contract in about the same time that a heart does placed in water; its appearance does not undergo any change.

5. The pupil of the frog's eye is not dilated by atropine, either when locally applied or injected under the skin.

6. The lymphatic hearts cease to contract long before the blood-heart.

*Digitaline*.—1. After the injection of about  $\frac{1}{60}$  gr. under the skin, the frog at first jumps about, then becomes quiet, sinks down on the plate, cannot be easily roused and dies in about from twenty to forty minutes. Sometimes the frog has paroxysms of gasping movements, lasting from twenty to fifty seconds, in which it holds its mouth wide open, leaning on its fore paws. These attacks are paroxysmal, whilst the embarrassment of the heart is continuous. On opening the frog, the heart is found motionless and usually unirritable, the ventricle being small and pale.

Where digitaline is put into the mouth it causes a great secretion of fluid; in cats the salivation is very marked.

2. Digitaline acts with great energy on the heart, throwing it into violent and disorderly contractions which quickly end in a cessation of movement. The first visible effect occurs a short time after the injection under the skin, and consists in a diminished range of the heart's movements; but the most marked alteration is a certain embarrassment and loss of smoothness in the heart's contractions, as if there were a want of coordination in the contractions of the individual fibres.

The ventricular systole presents a peculiar appearance and takes a longer time for its performance than in health; it appears to travel along, squeezing the heart up, as it were, and forcing the blood into one spot, which becomes bright red and projecting; at the same time there are prominent muscular bundles on the surface of the ventricle giving it an irregular motion.

During diastole, the ventricle does not everywhere assume a red colour, but one or more irregular red spots appear as if it were so firmly contracted as only to permit the entrance of a small quantity of blood. These spots become smaller and smaller, until at last the ventricle is left very pale, strongly contracted and motionless, whilst the auricles are distended with blood.

3. The frequency of the heart's contractions is not increased, but is progressively diminished.

4. The functions of the heart are abolished very early, voluntary power, as shown by the frog's ability to jump about with its heart motionless and contracted, reflex acts and the contractility of the lymphatic hearts surviving the death of that organ.

5. The rhythm of the heart's contractions is but little interfered with until near the end, when they become irregular in frequency and force.

6. Immersion of the heart, removed from the body, in a solution of digitaline causes the ventricle to become somewhat uneven in outline; the contractions get weak and infrequent and at last cease, sooner by some minutes than in a heart placed in water; the appearance of the ventricle when it has ceased to beat, presents little that is peculiar, except that it often looks uneven.

*Aconitine*.—1. After the injection under the skin of about  $\frac{1}{50}$  gr. the frog jumps about for a few minutes and then either sinks down on the plate, or else falls over on to its back, as if it had lost both muscular power and the ability to direct its movements; in either case it dies in from twenty to forty minutes. If the dose is larger, the frog falls as if stunned, almost immediately after the injection; from this state it partially revives, but dies at the end of a few minutes. On exposing the heart it is found beating, but rather feebly, and continues to do so for one or two hours.

2. When the heart is exposed *in situ*, aconitine is seen to have a very distinct and powerful action upon it. Its contractile power is quickly impaired giving rise to a peculiar perversion of rhythm. The interval of relaxation of the ventricle is considerably lengthened, whilst the auricles go on contracting regularly, the consequence is that the ventricle becomes more and more distended with blood, at last a limited part of it contracts, this area of contraction increases with each systole until, in time, the blood is forced, at each contraction, to one part of the heart which projects as a nodule, in a short time the whole ventricle becomes involved in contraction and empties itself in the ordinary way; soon after the ventricle again enters into a state of relaxation when the same series of acts is repeated. Finally, the ventricle is left large, dark and distended with blood, in a condition exactly contrary to that of a heart arrested by digitaline.

3. When a heart is removed from the body and immersed in a solution of aconitine it ceases to beat a little sooner than one does placed in water, but presents nothing peculiar in its appearance.

4. The frequency of the heart's pulsation is increased by a few beats at first, but in a short time there is a progressive diminution.

5. Although aconitine abolishes the functions of the heart in a comparatively short time, voluntary power, reflex acts and the contractility of the lymphatic hearts disappear some time before the blood-heart ceases to beat. The results obtained in about 170 experiments formed the basis for these conclusions.